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# Hydrophilic carbon nanoparticulates at the surface of carbon paste electrode improve determination of paracetamol, phenylephrine and dextromethorphan

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ABSTRACT

In this research, a novel carbon nanoparticles (Emperor 2000™)-modified carbon paste electrode (CNP/CPE) was fabricated and employed for determination of paracetamol (PA), phenylephrine (PHE) and dextromethorphan (DX) with good selectivity and high sensitivity. The paste design is based on (i) a hydrophobic binder, (ii) hydrophobic graphite as conductive component, and (iii) a thin film of nanoparticulate with hydrophilic surface to provide sensitivity and selectivity. Paracetamol, phenylephrine and dextromethorphan are frequently associated in pharmaceutical formulations against the common cold. Then determination of these compounds in a mixture is very important in pharmaceuticals and human fluids. CNP/CPE displayed excellent electrochemical catalytic activities towards paracetamol, phenylephrine and dextromethorphan oxidation. Using differential pulse voltammetry (DPV), a trace determination of PA, PHE and DX has been explored at the surface of modified electrode in presence of each other. Peak currents of PA, PHE and DX increased linearly with their concentrations at the ranges of $1.0 \times 10^{-7}$–$1.0 \times 10^{-3}$ M, $8.0 \times 10^{-6}$–$8.0 \times 10^{-5}$ M and $8.0 \times 10^{-6}$–$8.0 \times 10^{-4}$ M, and the detection limits were estimated $1.5 \times 10^{-8}$, $9.5 \times 10^{-7}$ and $2.9 \times 10^{-6}$ M, respectively. The modified electrode displayed strong function for resolving the overlapping voltammetric responses of PHE and DX into two well-defined voltammetric peaks. Method was applied successfully to the determination of PA, PHE and DX in real samples.



## 1. Introduction

Recently, carbon nanostructures have been employed in many applications such as sensing [1]. Various types of carbon nanomaterials such as nanotubes [2], graphenes [3], nanoparticles [4] and nanofibers [5] have been found wide interests because of owing to their unique physical and chemical properties which can provide an important and feasible platform for electroanalysis particularly in the design of modified electrodes for electrochemical sensing.

Commercial carbon blacks, Carbon nanoparticles (CNPs), are 1 to 50 nm in diameter with a high surface area accessible for chemical functionalization and ideal for effective interaction with redox active species [6]. Although these materials are structurally less well-defined in comparison to carbon nano-tubes or graphene materials, they offer many opportunities for new devices and technologies, for example, nano-carbon-based sensors [7,8]. CNPs, generally exhibit extremely high surface areas, high conductivity, and a multitude of reactive surface and adsorption sites [9]. CNPs may be considered more economical than other nano-carbons, as they are produced commercially in bulk quantities and also often formed as waste by-products during the formation of other nano-materials such as CNTs.

Carbon paste electrode (CPE) is a special kind of heterogeneous carbon electrode consisting of a mixture prepared from carbon powder and a suitable water-immiscible and non-conducting binder [10]. Chemically modified carbon-paste electrodes (CMCPEs) have attracted more interest due to their potential applications in various analyses [11]. These electrodes have been widely used in electroanalysis due to their ability to catalyze the redox processes of some molecules of interest, since they facilitate the electron transfer. CMCPEs are inexpensive and possess many advantages such as low background current, wide range of potential windows (in both cathodic and anodic region), easy fabrication, rapid surface renewal and modification compatibility with various modifiers such as mesopore materials [12], metal nanoparticles [13], carbon nanostructures [14] and enzymes [15].

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Paracetamol (PA) is an effective and widely used analgesic and antipyretic medicine with rather limited anti-inflammatory properties [16]. This substance is commonly used to deal with mild pain, including headache, backache, arthritis and postoperative pain, and has been recognized as a good alternative to aspirin [17]. In addition, PA is also a common ingredient of most kinds of commercial cold medicines. However, overdoses of PA may be toxic and lead to several side effects, including liver and kidney damages [18]. Therefore, it is important to develop a fast, convenient, low-cost and accurate method to detect PA. Several techniques have been developed to detect PA, including titrimetry [19], spectrophotometry [20], spectrofluorometry [21], chromatography [22], and capillary electrophoresis [23].

Dextromethorphan (DX) is the dextro-isomer of levorphanol and an analog of codeine and a semisynthetic morphine derivative [24]. It is an over-the-counter, highly effective antitussive drug that is widely prescribed for temporary relief of cough caused by minor throat and bronchial irritation [25] which it mainly acts on cough center in the medulla to treat mentioned respiratory disorders [26]. DX at higher dose has psychoactive properties similar to those of phencyclidine; hence it is abused in addicted people [27]. Several techniques have been developed to detect DEX alone or with other drugs such as LC–MS/MS [28], potentiometric sensor [29], spectrophotometry [30], capillary electrophoresis [31] and fluorimetry [32].

Phenylephrine (PHE) is a sympathomimetic drug used for nasal congestion, sinusitis and rhinitis. It is also used in ophthalmology as a mydriatic and conjunctival decongestant [33]. PHE has been previously determined in several pharmaceutical forms by flow injection analysis [34], spectrophotometry [35], HPLC [36], spectrofluorimetry [37], capillary electrophoresis [38], proton magnetic resonance [39].

Pharmaceutical formulations against the common cold use to contain compounds in very different proportion such as paracetamol, phenylephrine and dextromethorphan. Therefore, it is important that to develop a simple and sensitive method for the simultaneous determination of these drugs. Compared to other analytical techniques, electrochemical methods are simple, inexpensive, and easy to use. Table 1 compares some electrochemical methods which previously used for the determination of PA, PHE and DX [40–47]. As literature survey, there is no electrochemical method for simultaneous determination of PA, PHE and DX.

In this paper, for the first time tosyl carbon nanoparticles (CNP) has been applied for modifying carbon paste electrode (CNP/CPE). Modification has been performed by casting the microliter amount of CNP at the surface of CPE. The modified electrode is able to separate voltammetric peaks of paracetamol, phenylephrine and dextromethorphan. Finally, determination of PA, PE and DX at the surface CNP/CPE electrode in human serum and commercial samples is demonstrated.

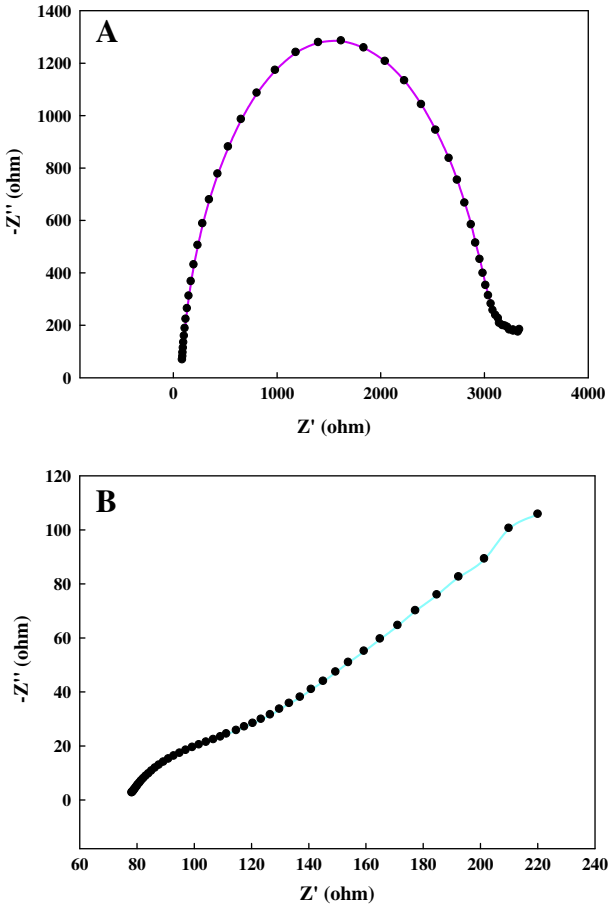


**Fig. 1.** Nyquist diagram (Z″ vs. Z′) for the EIS measurements in 1 mM $K_3Fe(CN)_6$/$K_4Fe(CN)_6$ + 0.1 M KCl at the formal potential 0.2 V for (A) CPE, (B) CNP/CPE. Potential: 0.2 V, frequency range: 1 Hz–10,000 Hz.

## 2. Experimental

### 2.1. Apparatus

Voltammetric experiments were performed using a Metrohm Computrace Voltammetric Analyzer model 797 VA. A conventional three-electrode system was used with a carbon paste electrode (3 mm diameter CPE), a KCl- saturated calomel reference electrode (SCE), and a Pt wire as the counter electrode. A digital pH/mV/Ion meter (Metrohm) was applied for the preparing of the buffer solutions, which were used as the supporting electrolyte in voltammetric experiments. Electrochemical impedance spectroscopic

**Table 1**
Comparison of some electrochemical methods which previously used for the determination of PA, PHE and DX.

| Analyte | Electrode | Modifier | DLR (μM) | LOD (μM) | Refs. |
|---|---|---|---|---|---|
| Paracetamol | GC | Graphene–chitosan composite | 1.0–200.0 | 0.3 | [40] |
| | GC | (Diglycolic acid) polymer | 0.2–500.0 | $6.7\times 10^{-3}$ | [41] |
| | GC | Graphite oxide film | 0.16–26.0 | 0.039 | [42] |
| | GC | Poly(taurine)/MWCNT | 1.0–100.0 | 0.5 | [43] |
| | GC | Polyaniline–MWCNT | 1.0–100.0 | 0.25 | [44] |
| | **CPE** | **Carbon nanoparticle** | **0.1–1000.0** | **0.015** | **This work** |
| Phenylephrine | CPE | Sodium-dodecyl sulfate | 0.04–100.0 | 0.0097 | [45] |
| | GC | MWCNT | 0.1–7.0 | 0.03 | [46] |
| | **CPE** | **Carbon nanoparticle** | **8.0–80.0** | **0.95** | **This work** |
| Dextromethorphan | CPE | CNT/ionic liquid composite | 250.0–3300.0 | 29.36 | [47] |
| | **CPE** | **Carbon nanoparticle** | **8.0–800.0** | **2.89** | **This work** |